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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,525	01/10/2001	Peng George Wang	10114/6	9752

757 7590 03/16/2006

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/758,525	WANG ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39,43,45-48 and 52-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39,43,45-48 and 52-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL REJECTION

1. Applicants' amendment and response filed February 2, 2006, is acknowledged. Claims 39, 43, 45-48 & 52-70 are pending and under consideration in this examination.

2. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

4a. ***Sequence Rules***

The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a) and (a)(2). However, the specification fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825 as follows: Applicants' submission of a hard copy "Sequence Listing" as required by 37 CFR § 1.821(d) as well as in computer readable form (CRF), filed November 4, 2004, is acknowledged. Appropriate corrections for compliance is required, which includes resubmission of the CRF and a hard copy of the sequence listing, along with a statement that the information contained in the hard copy and the CRF are identical.

CRF problem report enclosed previously, to aid the Applicants in the correction for sequence compliance.

CRF problem is related to Applicants' 'sequence listing' filed 10.22.2002, NOT November 4, 2004 as previously argued by the Applicants. Compliance is required.

Applicants' amendment and response filed February 2, 2006, do not respond to this requirement for compliance with the sequence rules.

4b. ***hyperlink***

The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, page 25 of Applicants'

amendment filed July 26, 2004, is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference.

Applicant's cooperation is requested in correcting all ***hyperlink(s)*** which may have been added or were present in the original specification at the time of filing.

5. Applicants argue that the present amendments are substantially as suggested by the Examiner. Claim 39 has been amended to narrow the types of cells used to practice the invention to *E. coli* lacZ and to yeast cells. Claim 39 and claims dependent therefrom have also been amended to recite an 'isolated cell', in accordance with the Examiner's assertion that this would clarify that the invention is directed towards bioengineered cells.

Applicants' amendment to claim 39 reciting a specific type of cell is noted. However, the key issues discussed during the telephonic interview on January 17, 2006, was that the Applicants' specification as enabling for the specific construct or 'superbug' (see the 112 first paragraph rejections) comprising specific genes from specific source. For example,and indicated in the enablement rejection - One of skill in the art can certainly use the instant specification as a guide to make and use a cell that produces glycoconjugates, but the question is to what extent. As explained in the enablement rejection guidance is limited to the construction of single super bug or isolated ***E. coli*** cell comprising (1) galactokinase (GalK), (2) galactose-1-phosphate uridylyltransferase (GalT), (3) glucose-1-phosphate uridylyltransferase (GalU) and (4) pyruvate kinase (PykF); and a glycosyltransferase, viz., (5) I1, 3-galactosyltransferase, all from **bovine**, for the production of α-galactose, an oligosaccharide. However, this is not quite what is reflected in Applicants' amendment.

6. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Claims 39, 43, 45-48 & 52-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell transformed with a nucleic acid encoding a sugar-nucleotide regenerating enzyme viz., (1) galactokinase (GalK), (2) galactose-1-phosphate uridylyltransferase (GalT), (3) glucose-1-phosphate uridylyltransferase (GalU) and (4) pyruvate kinase (PykF); and a glycosyltransferase, viz., (5) I1, 3-galactosyltransferase, all from *Bovine*, for the production of oligosaccharides (α-galactose), does not reasonably provide enablement for the transformation of host cell(s) using any or all the five 5 enzymes (as described above in 1-5) of the biosynthetic pathway for the formation of α-galactose from any source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 39, 43, 45-48 & 52-70 are so broad as to encompass a cell comprising one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase from any source for the production of any glycoconjugate, which may includes an oligosaccharide, a glycoprotein, a glycolipid, among others. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of sugar nucleotide regenerating enzyme(s) and glycosyltransferase(s), from any source, broadly encompassed by the claims.

The specification provides the construction of single super bug or cell comprising (1) galactokinase (GalK), (2) galactose-1-phosphate uridylyltransferase (GalT), (3) glucose-1-phosphate uridylyltransferase (GalU) and (4) pyruvate kinase (PykF); and a glycosyltransferase, viz., (5) I1, 3-galactosyltransferase, all from **bovine**, for the production of oligosaccharides (α-galactose).

The prior art describes the glycosyltransferases to be a large family of enzymes that participates in a concerted fashion in the biosynthesis of polysaccharides, and of carbohydrate moieties of glycoproteins and glycolipids. The

sequence-function relationship of this class of proteins in prokaryotes and Eukaryotes class of proteins has been recently reviewed [see Breton et al. J. Biochem. 123, 1000-1009 (1998), see abstract, **IDS**], The results of this study allowed the grouping of 12 groups of glycosyltransferases into 5 families. Using a conserved graphics method for protein comparison, conserved structural features were found in some of the glycosyltransferase groups, indicating lack of conserved sequences among the glycosyltransferase(s) family. Further distinction has been observed among the glycosyltransferases from Prokaryotes and Eukaryotes. In eukaryotes, glycosyltransferases consist of a short N-terminal cytoplasmic tail, a transmembrane domain, a stem region of variable length and a large C-terminal globular catalytic domain. This is in contrast to bacterial (prokaryotic) glycosyltransferases, some having several transmembrane domains, whereas others bind to membranes even though no membrane domains were predicted [see, Breton et al. (1998), page 1000, column 1-2]. The glycosyltransferases constitute a large heterogeneous class of enzymes, some families include enzymes that catalyze different reactions (see, Breton et al. concluding remarks on page 1007). Since the amino acid sequence of an enzyme determines its structural and functional properties, and because there appears to be a large variation among the different types of glycosyltransferases as well as the source from it is obtained, inserting these genes from any source into a cell construct will not only be undue but lead to transformed cell incapable of yielding the desired product in view of the different members of the enzyme catalyzing different reactions.

While recombinant techniques are known, it is <u>not</u> routine in the art to screen for multiple genes from a variety of sources, to obtain <u>sugar nucleotide regenerating enzyme</u> viz., Ga1k or GalT or GaIU or Pykf or Ndk or PpK or AcK or PoxB or Ppa or PgM or NagE or Agml or glmu or GalNAc kinase or pyrophosphorylase or Ugd or NanA or Cmk or NeuA or A1g2 or Algl or SusA or ManB or ManC or phosphomannomutase or Ga1E or GMP or GMD or GFS from

any source; **and/or** a glycosyltransferase enzyme from among · LgtB, LgtC (galactosyltransferase); Lgtf, Alg5 or DUGT (glucosyltransferase); LgtA (N-acetylglucosaminyl transferase); UDP-GalNAc:2'-fucosylgalactiside-I-3-N-acetylgalactosaminyl transferase; UGT2B7 (glucoronyltransferase); SiaT0160 (sialyltransfearse); Alg1 or Alg2 (mannosyltransferase); I 1,3-FucT or I 1,2-FucT or I 1,3,4-FucT (fucosyltransferases)] from any source and integrate into the genome of the cell, as encompassed by the instant claims, and/or transform any cell with these genes in various combination(s) irrespective of the biosynthetic pathway or sequential steps, to obtain the desired product would be highly unpredictable and with no reasonable expectation of success in obtaining the desired construct/ activity/product, because of insufficient guidance.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any cell comprising one or more sugar-nucleotide regenerating enzyme and one or more glycosyltransferase from any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of cell construct comprising equivalent sequence as relevant to the metabolic or biosynthetic pathway in question, and having the capability of producing the desired biological product(s) is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants' Arguments (previous):

Referring to various pages in the instant specification, Applicants argue that the specification can be used as a guide for one skilled in the art to make and use a cell that produces glycoconjugates.

One of skill in the art can certainly use the instant specification as a guide to make and use a cell that produces glycoconjugates, but the question is to what extent. As explained in the enablement rejection guidance is limited to the construction of single super bug or isolated ***E. coli*** cell comprising (1) galactokinase (GalK), (2) galactose-1-phosphate uridylyltransferase (GalT), (3) glucose-1-phosphate uridylyltransferase (GalU) and (4) pyruvate kinase (PykF); and a glycosyltransferase, viz., (5) I1, 3-galactosyltransferase, all from **bovine**, for the production of α-galactose, an oligosaccharide.

Applicants submit in Appendix A post-filing publications describing the creation of specific constructs and their expression in E. coli, predominantly. Applicants' claims are, however, not drawn to a small number of specific construct or the specific *E. coli* host cell comprising the specific genes, are therefore not enabling.

There is no guidance to transforming any type of *E. coli* or yeast cell (claims 39, 46-48 & 52-70) with an entire laundry list of genes (see claim 52, for example) from any source, some/many not yet characterized. Further, reasons are as explained in the rejection, not responded to by the Applicants. The rejection is therefore maintained.

Applicants' Arguments (present):

Applicants argue that the specification can be used as a guide for one skilled in the art to make and use a cell that produces glycoconjugates, and point to the description or availability of the genes for: (1) sugar-nucleotide regeneration (*see* Applicants' amendment on page 7), including UDP-Gal, UDP-Glc..... GDP-Fuc; (2) glycosyltransferase (specific pages and lines in the specification are referred to), and how the glycosyltransferases from among members of the same family share sequence identities and similarities, as well the knowledge of the crystal structure.

Furthermore, Applicants argue, that in the examples shown in the patent application [a host cell transformed with a nucleic acid encoding sugar-nucleotide

regenerating enzymes viz., (1) galactokinase (GalK), (2) galactose-l-phosphate uridylyltransferase (GalT), (3) glucose-l-phosphate uridylyltransferase (GalU), and (4) pyruvate kinase (PykF), and a glycosyltransferase, viz. (5) al,3-galactosyltransferase (from bovine) for the production of oligosaccharides (e.g. a-galactose), the al,3-galactosyltransferase used was cloned from **bovine**; it was not from E. coli. Applicants' correction is noted and changes have been made according in the enablement rejection.

The superbug of Example 2 contained an a1,4GalT gene from *Neisseria meningitidis*, gram-negative diplococcus (page 57, lines 5-15).

The superbug of Example 3 contained a sucrose synthase gene from Anabaena sp., a cyanobacterium (page 62, lines 8-10), and an al, 3-galactosyltransferase from **bovine**.

As noted above the superbug in example 1 produces galactose, an oligosaccharide (or a **glycoconjugate**).

Applicants' claims are directed to a cell for the production of any **glycoconjugate** based upon the production of a single glycoconjugate – a galactose. Applicants have failed to explain how the production of a single glycoconjugate – a galactose, would be sufficiently enabling for one skilled in the art to produce any glycoconjugate using genes from any source based upon the example of bovine genes of example 1.

While several of these genes are known from a variety of sources, and that the various metabolic pathways are described, however, selective yeast or *E. coli* constructs comprising genes from any source in order to produce any glycoconjugate of interest, require more than mere existence of genes and/or knowledge of pathways. These include the isolation of these genes from any source, selective optimization of the cell constructs, knowledge of enzyme kinetics as effected by the new environment of the host, etc., in order that a skilled artisan be able to extrapolate the guidance of working examples 1, 2 and 3, to the level claimed. The

bovine genes used in the *E. coli* or yeast cell construct of example 1, 2 & 3, as disclosed by the Applicants is not representative or enabling for the scope claimed.

Applicants' further evidence that the invention can be realized as described in the specification. Applicants submitted on June 23, 2005 an Appendix A containing post-filing publications by one or more of the co-inventors describing the use of the methods for creation of different prokaryotic and eukaryotic superbugs producing: alpha-ES in *E. coli* (Chen et al., 2001, J Am. Chem. Soc. 123: 8866-8867); αKTUF in E. coli (Chen et. al., 2002, ChemBiochem 3: 47-53); CKTUF in *E. coli* (Zhang et al.., 2003, Org. Biomolecular Chem. 1: 3048-3053); and SEα in yeast (Shao et al., 2003, Appl. Environ. Microblèl. 69: 5238-5242).

No copies of these references have been received in order that Applicants' arguments be considered.

7. Claims 39, 43, 45-48 & 52-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 39, 43-48 & 52-70, recite a *E. coli* or yeast cell comprising one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase from any source for the production of any glycoconjugate, which may includes an oligosaccharide, a glycoprotein, a glycolipid, among others. More specific recitation includes a cell comprising sugar nucleotide regenerating enzyme comprising, Galk or GalT or GalU or Pykf or Ndk or PpK or AcK or PoxB or Ppa or PgM or NagE or Agml or glmu or GalNAc kinase or pyrophosphorylase or Ugd or NanA or Cmk or NeuA or A1g2 or Algl or SusA or ManB or ManC or phosphomannomutase or GalE or GMP or GMD or GFS from any source; **and/or** a glycosyltransferase enzyme comprising – LgtB, LgtC (galactosyltransferase); Lgtf, Alg5 or DUGT (glucosyltransferase); LgtA (N-acetylglucosaminyl transferase); UDP-GalNAc:2'-

fucosylgalactiside-I-3-N-acetylgalactosaminyl transferase; UGT2B7 (glucoronyltransferase); SiaT0160 (sialyltransfearse); Alg1 or Alg2 (mannosyltransferase); I 1,3-FucT or I 1,2-FucT or I 1,3,4-FucT (fucosyltransferases)] from any source.

The specification, however, only provides a single representative species - in the construction of single super bug or cell comprising (1) galactokinase (GalK), (2) galactose-1-phosphate uridylyltransferase (GalT), (3) glucose-1-phosphate uridylyltransferase (GalU) and (4) pyruvate kinase (PykF); and a glycosyltransferase, viz., (5) I1, 3-galactosyltransferase, all from *E.coli*, for the production of oligosaccharides (α-galactose). There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species. The specification also fails to describe additional representative species of these superbugs by any identifying structural characteristics other than the properties or activity recited in claims, for which no predictability of structure is apparent. Given this lack of additional representative species of these superbugs, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Therefore, the written description requirement is not satisfied.

Applicants' arguments:

Applicants argue that the specification is replete with examples having given activities that may be used together to regenerate sugar nucleotides, and figures providing diagrams of plasmids that are useful in creating the cells of the present claims. The sequences of thousands of sugar nucleotides regenerating enzymes, epimerases, and glycosyltransferases were known in the art at the time of filing. Moreover, the specification provides several working examples of cells of the present invention that produces a glycoconjugate of interest in the absence of an

exogenously supplied nucleotide triphosphate and comprises heterologous genes encoding one or more sugar nucleotide regenerating enzyme and one or more glycosyltransferase.

Clearly in the sequence data bases numerous sequences are known. However, the question is how representative are these sequences and the specific *E. coli* constructs comprising the specific enzymes from specific sources to genus being claimed? It is impossible to extrapolate the small set of species description to include a broad genus claimed. There is no description in the specification supportive of transforming *E. coli* or yeast cell with an entire laundry list of genes (see claim 52, for example) from any source, some/many not yet characterized. The rejection is therefore maintained.

8. Claim 48 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 47. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 39, 45, 47-48 and 52 are rejected under 35 U.S.C. 102(e) as being anticipated by Renkonen et al. (PGPUB 20020058313, September 26, 2000).

Claim 39 is drawn to an isolated *E. coli* or yeast cell that produces a glycoconjugate of interest[1], the cell comprising heterologous genes encoding one or more 'sugar nucleotide regenerating enzyme[2]' and one or more 'glycosyltransferase[3]'. Claim 47, adds the limitation wherein the genes are encoded within one or more plasmids.

Renkonen et al. teach a process for preparing fucosylated glycans[1] (a glycoconjugate, see claim 1-6), by cultivating a yeast cell or *E. coli* (a single cell) which is transformed with the DNA sequence for GDP-mannose-4, 6-dehydratase[2] (a sugar nucleotide regenerating enzyme) and wherein the fucosylated glycans are prepared by recombinant alpha 1, 3-fucosyltransferase (a glycosyltransferase[3]) using the DNA encoding alpha 1, 3-fucosyltransferase (*see* claims 7 & 31 of the PGPub and the entire patent). No nucleotide triphosphate is supplied exogenously. The reference teaching all the limitations anticipates the claims.

10. ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43, & 53-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Renkonen et al. (PGPUB 20020058313, September 26, 2000), Koizumi et al. [Koizumi et al. (1998) Nature Biotechnology, 16: 847-850] and Borge et al. [Gene 223:213-219 (1998)]. The teachings of Renkonen et al. are described above in paragraph 9. Renkonen et al. do not teach limitations of claims 43, 46 & 53-70.

Koizumi et al. teach that the production of globotriose (oligosaccharides) was accomplished by coupling a combination of cell constructs – *E. coli* cells transformed with sugar nucleotide regenerating enzyme *galT, GalK,* and *GalU,* and with a glycosyltransferase such as, alpha 1,4-galactosyltransferase gene (lgtC); and where in the cells produces a glycoconjugate, such as globotriose, in the absence of exogenously supplied nucleotide triphosphate. Expression of various genes of interest, viz. 'sugar nucleotide regenerating enzyme' and a 'glycosyltransferase' in a single cell is lacking.

Borge et al. teach a simple and rapid procedure for gene or group of genes to be integrated into the genome of the cell and which can be inserted into a multiple

cloning site, flanked by an antibiotic resistance marker and *lacZ* gene of *E. coli.* (claim 46).

Applicants on page 7 of their response, for example, admit that genes encoding sugar nucleotide encoding enzymes (see specification on page 10, lines 14-16); and gene encoding glycosyltransferases (see specification on page 21, lines 13-18), are well known in the art.

It would have been obvious to one of ordinary skill in the art, at the time the invention was made to take advantage of the single cell system of Renkonen et al. as compared to the two cell system of Koizumi for the expression of genes of interest, viz. 'sugar nucleotide regenerating enzyme' and a 'glycosyltransferase' the production of glycoconjugates in view of the demonstrated ease of operation and convenience for the production of glycoconjugates in a single cell. The technique of gene integration is well established in the art and enjoys the advantages of avoiding the problem of gene segregation, instability and undesired copy number effects which are associated with autonomously replicating plasmid vectors (Borgne, 1998), and is therefore a preferred choice.

One of ordinary skill in the art would have had a reasonable expectation of success in preparing *E. coli* or yeast cell construct(s) comprising specific 'sugar nucleotide regenerating enzyme' and a 'glycosyltransferase' genes taught by Koizumi et al. or those *specific* genes from *specific* sources (*or organism*) available and well known in the prior art.

One of ordinary skill in the art would have been motivated to prepare the cell constructs for the production of desired glycoconjugate(s) in view of well known and documented use of the glycoconjugate(s), such as fucosylated glycans in the treatment of inflammatory responses (*see* Renkonen et al.). They can be used to block leukocyte traffic to sites of inflammation and thus reduce or otherwise ameliorate an undesired inflammatory response and other disease states characterized by a leukocyte infiltrate. They are also useful in blocking bacterial

adherence to endothelium and thus they prevent and/or treat bacterial infections. A further use of the fucosylated glycans lies in the field of cancer treatment where metastasis of tumor cells can be inhibited by these glycans.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, *prima facie* obvious.

9. No claim is allowed.

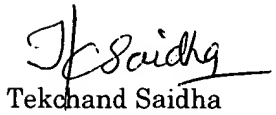
10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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